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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/762,154	**Applicant(s)** NEZU ET AL.	
	Examiner Bridget E. Bunner	**Art Unit** 1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 February 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *26 March 2008*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, 36*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Bridget E Bunner/
Primary Examiner, Art Unit 1647

Continuation of 11. does NOT place the application in condition for allowance because:

1. Claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, and 36 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Applicant's arguments (25 February 2008) as they pertain to the rejection have been fully considered but are not found to be persuasive.

At the bottom of page 7 of the Response, Applicant states that the specifcation asserts at least one credible, specific and substantial utility, namely, screening for carcinostatic compounds that are transported by hOCTN1 (page 31, lines 5-16). Applicant argues that the specification teaches that the encoded hOCTN1 polypeptide contains the structural features of a well-known class of proteins, organic cation transporters. Applicant indicates that the working examples in the specification demonstrate hOCTN1-mediated transport of a variety of compounds, including carcinostatics, such as actinomycin D, etoposide, vinblastine, and daunomycin. Applicant argues that the specification teaches the distribution of the hOCTN1 organic cation transporter in a variety of cells and tissues, including its prevalence in tumor cell lines. At the bottom of page 8 of the Response, Applicant contends that the utility for the claimed nucleic acids is expressing the encoded hOCTN1 tranporter proteins in cells and screening for carcinostatics that are preferentially absorbed and transported by hOCTN1. Applicant submits that the screen permits the selection of carcinostatics that will be absorbed by target tissues or cells that express the hOCTN1 transporter. Applicant states that if one is trying to treat a cancer in which the cells express the hOCTN1 transporter, one can use the screen to identify which of a number of potential carcinostatics would be most effectively taken up by these cells.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, as discussed in the prior office actions, the instant specification does not teach any physiological significance or functional characteristics of the OCTN1 polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotides and polypeptide of the instant invention are involved in any specific activity. There is no biological activity, phenotype, disease or condition, binding partner, or any other specific feature that is disclosed as being associated with OCTN1. The specification of the instant application only teaches that hOCTN1 is present in a few cancer cell lines, such as HeLa S3, K562, SW480, and A549 (page 24, lines 1-21). There is no evidence in the specification or the prior or post-filing art indicating that hOCTN1 is associated with or has altered expression in cancer cells isolated from tissue as compared to a normal control. Although the hOCTN1 protein of the instant application is able to transport carcinostatics, the physiological function of the protein has yet to be determined. Additionally, Applicant's asserted utility of screening for carcinostatics is not specific or substantial. Such assays can be performed with any polypeptide. The specification discloses nothing specific or substantial for the compounds screened in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Whereas a scale or a microarray or a gas chromatograph has patentable utility as a research tool, the objects being evaluated with those research tools do not necessarily have patentable utility. In the instant case, the claimed hOCTN1 nucleic acid molecules and encoded polypeptides are not disclosed as having an activity that can be specifically useful. Thus, further research is required to identify or reasonably confirm a specific and substantial utility. MPEP §2107(I)(C) even states that "[l]abels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention". The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA (see In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court held that §101 requires a utility that is both substantial and specific. The court held that a "[p]atent application does not satisfy utility requirement of 35 U.S.C. §101 unless it discloses both "substantial" utility for claimed invention, in form of significant and presently available benefit to public, as well as "specific" utility, which is well-defined and particular benefit to public". Furthermore, in Brenner v. Manson, the court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility.

At pages 7 and 9 of the Response of 25 February 2008, Applicant states that during the inteview of January 10, 2008, the Examiner based her assertion of a specific and substantial utility for a newly discovered protein on several recent unpublished decisions by the Board of Patent Appeals and Interferences. At pages 11-14, Applicant cites several decisions. The Examiner would like to reiterate to the Applicant that the Examiner's rejection of the instant claims is based upon 35 U.S.C. § 101 and not upon unpublished decisions by the Board of Patent Appeals and Interferenes. The current rejection is in compliance with the most currently-published version of the Utility Guidelines which require that all biological inventions must have a credible, specific, and substantial ("real world" utility). The Examiner simply mentioned during the interview that the Board of Patent Appeals and Interferences had rendered several decisions regarding the utility of novel molecules, such as transporters and receptors. The Examiner did not state any specific application numbers, as each application is examined on its own merits. It is also noted that the opinions in support of the decisions of the Board of Patent Appeals and Interferences in the cases cited by Applicant were not written for publication and are not binding precedent of the Board.

As discussed in the previous Office Action, the post-filing date study of Tamai et al. (FEBS Letters 419 : 107-111, 1997), co-authored by the inventors of the instant application, discloses an isolated nucleic acid encoding the organic transporter protein comprising the amino acid sequence of SEQ ID NO: 1 of the instant application. The reference states that OCTN1 "was found in several human cancer cell lines as well as in normal kidney, bone marrow and trachea, although its physiological role in these tissues remains to be established. Further studies, including subcellular localization using antibody and elucidation of the mechanism of the pH dependence and metabolic energy-sensitive activity, as well as the substrate specificity, are needed to establish the physiological importance of this transporter" (page 111, column 2, last paragraph). Hence, although OCTN1 may transport various organic cations, its physiological role remains to be elucidated.

2. Claims 8, 10, 11, 13, 16, 18-21, 23-25, 27, 32, 36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

3. Claims 10, 18, 23, and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. At page 17 of the Response, Applicant argues that the variant sequences described in the specification (50%, 54%, and 76% homologous to hOCTN1) have organic cation transporter activity, thus evidencing possession of functional organic cation transporters that share far less than 95% sequence identity with hOCTN1. Applicant's arguments (25 February 2008) as they pertain to the rejection have been fully considered but are not found to be persuasive. The specification of the instant application does not disclose which 1 to 30 amino acids can vary from SEQ ID NO: 1 and still result in a protein that retains the ability to transport an organic cation. The specification does not teach which of the nucleic acid sequences that encode a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 with one to 30 conservative amino acid substitutions encode a polypeptide having the required activity of transporting an organic cation. The description of one human OCTN1 nucleic acid (SEQ ID NO: 2) and one mouse OCTN1 nucleic acid (SEQ ID NO: 23) is not adequate written description of an entire genus of functionally equivalent nucleic acids that encode polypeptides with 1 to 30 conservative amino acid substitutions in SEQ ID NO: 1, wherein the polypeptide is an organic cation transporter. The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of nucleic acid molecules and polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function.

4. The rejection of claims 8, 10, 16, 18, 21, 23, 27, 29-31, 32 under 35 U.S.C. § 112, first paragraph (scope of enablement) is withdrawn in view of the amended and cancelled claims.

5. The rejection of claims 8, 16, 21, 27, 29-31 under 35 U.S.C. § 112, first paragraph (written description) is withdrawn in view of the amended and cancelled claims.